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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/811,138	03/29/2004	Sylvia Daunert	50229-421	8471

7590 04/26/2007

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EXAMINER	
KOSSON, ROSANNE	
ART UNIT	**PAPER NUMBER**
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/811,138	DAUNERT ET AL.	
	Examiner	Art Unit	
	Rosanne Kosson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-53* is/are pending in the application.

4a) Of the above claim(s) *1-11 and 14-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 September 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on April 2, 2007 has been received and entered. Claims 12 and 13 have been amended. No claims have been canceled or added. Claims 1-11 and 14-53 were withdrawn in the previous Office action as being drawn to non-elected inventions. Accordingly, claims 12 and 13 are examined on the merits herewith.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112, first paragraph

Claims 12 and 13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims have been amended to recite a polynucleotide "having at least 95% similarity to SEQ ID NO: 3 under stringent conditions" and that encodes a functional Y-to-W or Y-to-F substitution mutant of SEQ ID NO: 4 at amino acid position 82. The phrase "having at least 95% similarity to SEQ ID NO: 3 under stringent conditions" does not appear in the specification. Page 17 mentions the terms stringent hybridization conditions and % sequence identity, but not the term or concept of % similarity under stringent conditions. THIS IS A NEW MATTER REJECTION. New matter is prohibited, and Applicants are required to cancel new matter from the claims (see MPEP 608.04).

Claims 12 and 13 are again rejected under 35 U.S.C. 112, first paragraph, because the

specification, while being enabling for the polynucleotide of SEQ ID NO: 3 in which position numbers 347-348 are mutated from AT to GG or TC or TT to produce the Y-to-W or Y-to-F amino acid mutation (one or two point mutations in this codon), does not reasonably provide enablement for any polynucleotide that has "95% similarity to SEQ ID NO: 3 under stringent conditions" and that encodes a protein that is "capable" of binding coelenterazine and oxygen and emitting light and that has a W or F at amino acid position 82 of SEQ ID NO: 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The protein of SEQ ID NO: 4 and its variants with W or F at position 82 are functional aequorins, and the specification does not disclose, apart from the claimed mutations, how else the polynucleotide and polypeptide sequences may be mutated to produce the invention of claims 12-13. This rejection was discussed in the previous Office action with respect to polynucleotides that are "capable" of hybridizing to SEQ ID NO: 3 under stringent conditions and that encode a protein that is "capable" of binding coelenterazine and oxygen and emitting light and that has a W or F at amino acid position 82 of SEQ ID NO: 4.

In response to this rejection, Applicants have broadened the claims. Rather than reciting a polynucleotide capable of hybridizing under stringent conditions to SEQ ID NO: 3, the claims now recite a polynucleotide having 95% similarity to SEQ ID NO: 3 under stringent conditions. The amendment introduces a new two-fold problem. First, the Office does not recognize the term "% similarity" in connection with polynucleotide or polypeptide sequences, because this term has no clear meaning and, consequently, cannot enable the claimed invention. The Office recognizes and uses the term is "% identity" or "% sequence identity," because this claim language is clear and defines a sequence that can be searched. When comparing one sequence to another, the nucleotide or amino acid at each position in the chain is the either

same or different. Any nucleotide at a particular position in the chain is similar to other nucleotides. Thus, this limitation removes meaning from the claims and recites polynucleotides that are not enabled by the specification. Second, the concept of % similarity under stringent conditions, or even % identity under stringent conditions, has no clear meaning and does not enable the claims, because the degree to which two sequences are the same or different (the % of the nucleotides that are the same) is separate from and has nothing to do with the hybridization conditions. Changing the hybridization conditions does not make two sequences more or less identical or "similar." This concept mixes apples and oranges.

Regarding Applicants' remarks, Applicants assert that each part of the enablement rejection is a conclusion, Applicants disagree with the conclusions, and Applicants assert that no evidence has been provided.

In reply, Applicants have not specifically responded to the rejection. To reiterate, the rejection (relative to the previous claim language, for the sake of using claim language that is defined) is that Applicants claim the genus of a polynucleotide that is capable of hybridizing to SEQ ID NO: 3 under stringent conditions and that encodes a functional variant of SEQ ID NO: 4 in which the amino acid at position 82 is mutated to W or F, but only two species of this vast genus are disclosed. No structural information relative to SEQ ID NO: 3 or 4 is provided, with or without experimental data, i.e., which domains and which amino acids are critical for function and which are dispensable. No information is provided as to where and how and to what extent one of skill in the art may mutate SEQ ID NO: 4 having a mutation at position 82 so that the desired structural and functional properties will be retained. This missing information is the guidance that is missing from the specification. Without this guidance, it cannot predicted that the claimed but undisclosed species exist or can be made or that they will function the same way that the disclosed species do. Because the claimed but undisclosed species cannot be

predicted, the experimentation required to identify them is random and trial-and-error, and, therefore, the amount of experimentation required is undue. Applicants have not pointed out where the missing guidance can be found.

As for the Bryan reference, it is clear in the previous Office action that this reference was cited to show the state of the art. It is not a conclusion. Why undue experimentation is required was explained previously and is reiterated above, i.e., because a very large genus is claimed, only two species are disclosed and guidance to fill the gap has not been provided.

Regarding stringency and the hybridization and washing conditions, Applicants state at the bottom of p. 14 of their Response that no evidence has been presented to support a conclusion that one skilled in the art would consider Applicants' hybridization conditions to be of high stringency. Applicants appear to argue that one of skill in the art would not consider Applicants' hybridization conditions to be highly stringent. Nevertheless, the point in the previous Office action was that the room-temperature washing conditions are not highly stringent. Current Protocols in Molecular Biology (Ausubel et al., eds., Unit 6.3, John Wiley & Sons, Inc., Hoboken, New Jersey, 1993) notes on p. 6.3.6 that washing at low stringency is a straightforward proposition and is performed by adding the washing buffer at room temperature and washing at room temperature (see left col.). The previous page, p. 6.3.5, discusses that the stringency of the hybridization and washing conditions affect the signal-to-noise ratio of what binds to a particular DNA sequence and that, the lower the stringency, the higher the background (the noise). A larger amount of mis-matched nucleotides bind under low-stringency conditions. Thus, Current Protocols confirms that the room-temperature washing step does not correspond to stringent conditions.

In view of the foregoing, the holding of lack of enablement is maintained.

Claim Rejections - 35 USC § 112, second paragraph

Claims 12-13 are again rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims have been amended to recite a polynucleotide "having at least 95% similarity to SEQ ID NO: 3 under stringent conditions." As discussed above, this amendment presents a two-fold problem because, first, the Office does not recognize the term "% similarity" in connection with polynucleotide or polypeptide sequences. The Office uses the term "% identity" or "% sequence identity," because this claim language has a clear meaning and defines a sequence that can be searched. When comparing one sequence to another, the nucleotide or amino acid at each position in the chain is the either same or different. Any nucleotide at a particular position in the chain is similar to other nucleotides. Thus, the amended claim language removes any clear meaning from the claims, rendering them confusing and unclear, as it cannot be determined which polynucleotides Applicants mean to claim. Clear language is required.

Second, the concept of % similarity under stringent conditions, or even % identity under stringent conditions, has no clear meaning, because the degree to which two sequences are the same or different (the % of the nucleotides that are the same) is separate from and has nothing to do with the hybridization conditions. Changing the hybridization conditions does not make two sequences more or less identical or "similar." That is, changing the hybridization conditions does not alter a primary sequence. Of course, two sequences that have a high % sequence identity will hybridize under a wider range of conditions than two sequences that have a low % sequence identity. But, hybridization under stringent conditions and % sequence identity are distinct and separate concepts. Applicants' concept mixes apples and oranges and renders the

claims confusing and unclear. Terminology that the Office recognizes is "% sequence identity" (a sequence having a particular % sequence identity to SEQ ID NO: 3) and "hybridizes under highly stringent conditions" (a sequence that hybridizes under highly stringent conditions to SEQ ID NO: 3). Appropriate correction is required.

Regarding the term "stringent conditions," Applicants assert that these are defined on p. 18 and that broad is not indefinite. In reply, as previously discussed, the specification does not define or disclose stringent conditions, nor does it disclose any polynucleotides that bind under stringent conditions to SEQ ID NO: 3, regardless of what proteins they encode. Page 18 discloses what Applicants' conditions "involve." But, as discussed previously and above, the involved conditions are considered to be high-stringency hybridization conditions and low-stringency washing conditions. The rejection is that Applicants have not defined and have not used highly stringent conditions, nor have they disclosed any polynucleotides obtained under their conditions, apart from the two variants of SEQ ID NO: 3 that encode a substitution at amino acid position no. 82. The rejection is not that Applicants' claims are overly broad, but that they are unclear.

In view of the foregoing, the rejection for indefiniteness is maintained.

No claim is allowed.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosanne Kosson whose telephone number is 571-272-2923. The examiner can normally be reached on Monday-Friday, 8:30-6:00, alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rosanne Kosson
Examiner, Art Unit 1652

rk/2007-04-24

Rosanne Kosson

REBECCA E. PROUTY
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GROUP ~~1800~~ 1600